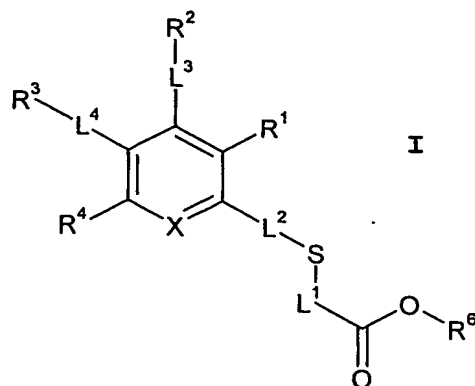


Claims

1. A compound of formula I:



wherein

5 X is N or CH;

R¹ is H, cyano, halo, hydroxy, hydroxamic acid, sulfhydryl or -NH₂; or C₁₋₄ alkyl optionally substituted by cyano, halo, hydroxy, hydroxamic acid, sulfhydryl or -NH₂; or -OR, -NHR, -NR₂ or -SR wherein R is C₁₋₄ alkyl optionally substituted by cyano, halo, hydroxy, hydroxamic acid, sulfhydryl or -NH₂;

R² is H, CF₃; or optionally substituted C₅₋₆ aryl, C₃₋₇ cycloalkyl, C₅₋₇ heterocyclyl or together with R³ an optionally substituted C₃₋₄ alkylene group wherein L³ and L⁴ are single bonds thus forming a C₅₋₆ ring fused with the aromatic ring to which L³ and L⁴ are attached;

R³ is H; or optionally substituted C₅₋₆ aryl, C₃₋₇ cycloalkyl, C₅₋₇ heterocyclyl or together with R² an optionally substituted C₃₋₄ alkylene group wherein L³ and L⁴ are single bonds thus forming a C₅₋₆ ring fused with the aromatic ring to which L³ and L⁴ are attached;

R⁴ is H; or optionally substituted C₅₋₆ aryl or C₅₋₇ heterocyclyl;

R⁶ is selected from H or optionally substituted C₁₋₇ alkyl, C₅₋₆ aryl and C₁₋₄ alkylene-C₅₋₆ aryl;

L¹ is optionally substituted C₁₋₄ alkylene, C₅₋₆ arylene,

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C₁₋₄ alkylene-C₅₋₆ arylene or -L⁵N(R⁵)L⁶-, wherein L⁵ and L⁶ are independently selected from optionally substituted C₁₋₄ alkylene and C₅₋₆ arylene, and R⁵ is H or C₁₋₄ alkyl;

5 L² is a single bond; or optionally substituted C₁₋₄ alkylene or -L⁷C(=O)L⁸-, wherein L⁷ and L⁸ are independently selected from optionally substituted C₁₋₄ alkylene and a single bond; and

10 L³ and L⁴ are independently selected from a single bond, optionally substituted C₁₋₄ alkylene, -L⁹YN(OH)C(=O)L¹⁰- and -L⁹C(=O)N(OH)YL¹⁰-, wherein L⁹ and L¹⁰ are independently selected from optionally substituted C₁₋₄ alkylene, C₅₋₆ arylene, C₁₋₄ alkylene-C₅₋₆ arylene and a single bond, wherein Y is NH or a single bond; or a pharmaceutically acceptable salt thereof for use in a
15 method of therapy.

2. A compound according to claim 1 wherein R¹ is chosen from the group consisting of H and cyano.

20 3. A compound according to any one of the preceding claims wherein R⁶ is H or C₁₋₇ alkyl.

25 4. A compound according to any one of the preceding claims wherein L¹ is chosen from the group consisting of phenylene, -CH(Ph)-, -CH₂-phenylene- and -CH₂C(=O)NH-phenylene-.

30 5. A compound according to any one of the preceding claims wherein L² is a single bond or -C(=O)CH₂-.

6. A compound according to any one of the preceding claims wherein L³ is chosen from the group consisting of a single bond, -L⁹YN(OH)C(=O)L¹⁰- and -L⁹C(=O)N(OH)YL¹⁰-,

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wherein L^9 and L^{10} are independently selected from optionally substituted C_{1-4} alkylene, C_{5-6} arylene, C_{1-4} alkylene- C_{5-6} arylene and a single bond, and wherein Y is NH or a single bond.

5

7. A compound according to claim 6 wherein L^3 is a single bond.

8. A compound according to any one of the preceding
10 claims wherein L^4 is chosen from the group consisting of a single bond, $-L^9YN(OH)C(=O)L^{10}-$ and $-L^9C(=O)N(OH)YL^{10}-$, wherein L^9 and L^{10} are independently selected from optionally substituted C_{1-4} alkylene, C_{5-6} arylene, C_{1-4} alkylene- C_{5-6} arylene and a single bond, and wherein Y is NH or a single
15 bond.

9. A compound according to claim 8 wherein L^4 is selected from the group consisting of $-CH_2N(OH)C(=O)-$,
-phenylene- $CH_2N(OH)C(=O)-$, -phenylene- $NHN(OH)C(=O)-$ and
20 $-CH_2C(=O)N(OH)-$.

10. A compound according to any one of the preceding claims wherein X is CH.

25 11. A compound according to claim 10 wherein one of R^1 , R^2 and R^4 are H.

12. A compound according to claim 10 wherein two of R^1 , R^2 and R^4 are H.

30

13. A compound according to claim 10 wherein R^1 , R^2 and R^4 are all H.

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14. A compound according to claim 10 wherein one of R^2 and R^3 is optionally substituted C_{5-6} aryl, C_{3-7} cycloalkyl or C_{5-7} heterocyclyl.

5 15. A compound according to claim 14 wherein R^3 is optionally substituted C_{5-6} aryl, C_{3-7} cycloalkyl or C_{5-7} heterocyclyl.

10 16. A compound according to claim 14 wherein R^3 is optionally substituted phenyl or C_{3-7} cycloalkyl.

17. A compound according to claim 14 wherein R^3 is phenyl or cyclopentyl.

15 18. A compound according to claim 10 wherein L^1 is phenylene or $-CH(Ph)-$.

20 19. A compound according to claim 10 wherein one of L^3 and L^4 is a single bond.

20. A compound according to claim 19 wherein L^3 is a single bond.

25 21. A compound according to any one of claims 1 to 9 wherein X is N.

22. A compound according to claim 21 wherein R^1 is cyano or hydroxamic acid.

30 23. A compound according to claim 21 wherein R^2 is selected from the group consisting of optionally substituted C_{5-6} aryl, C_{5-7} heterocyclyl, CF_3 and, together with R^3 , an optionally substituted butylene group wherein L^3 and L^4 are

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single bonds thus forming a C₆ ring fused with the aromatic ring to which L³ and L⁴ are attached.

24. A compound according to claim 23 wherein R² is
5 selected from optionally substituted C₅₋₆ aryl or C₅₋₇ heterocyclyl.

25. A compound according to claim 23 wherein R² is
10 selected from optionally substituted phenyl or thiophenyl.

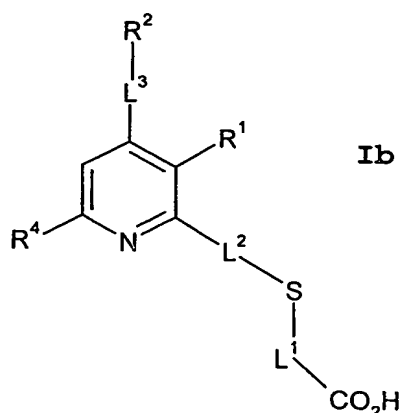
26. A compound according to claim 23 wherein R² is
selected from the group consisting of thiophenyl, phenyl,
p-chlorophenyl, p-methoxyphenyl, o-methoxyphenyl and
p-fluorophenyl.

27. A compound according to any one of claims 23 to 25
15 wherein R² is a monosubstituted phenyl group with the
substituent group being in the para position.

28. A compound according to any one of claims 21 to 27
20 wherein R³ is H or, together with R², an optionally
substituted butylene group wherein L³ and L⁴ are single
bonds thus forming a C₆ ring fused with the aromatic ring to
which L³ and L⁴ are attached.

29. A compound according to claim 28 wherein R³ is H and
25 L⁴ is a single bond such that the compound is of formula **Ib**:

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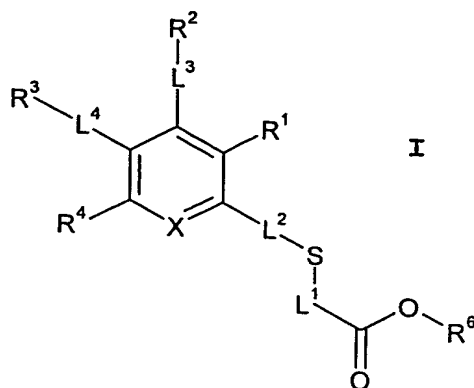
30. A pharmaceutical composition comprising a compound according to any one of the preceding claims or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable carrier or diluent.

31. Use of a compound according to any one of claims 1 to 29 or a pharmaceutically acceptable salt thereof in the preparation of a medicament for the treatment of a condition alleviated by inhibition of glyoxalase I.

32. A method of treating a condition which can be alleviated by inhibition of glyoxalase I, which method comprises administering to a patient in need of treatment an effective amount of a compound according to any one of claims 1 to 29, or a pharmaceutically acceptable salt thereof.

33. A compound of formula I:

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or a salt, solvate or chemically protected form thereof wherein

X is N or CH;

5 R^1 is H, cyano, halo, hydroxy, hydroxamic acid, sulfhydryl or $-NH_2$; or C_{1-4} alkyl optionally substituted by cyano, halo, hydroxy, hydroxamic acid, sulfhydryl or $-NH_2$; or $-OR$, $-NHR$, $-NR_2$ or $-SR$ wherein R is C_{1-4} alkyl optionally substituted by cyano, halo, hydroxy, hydroxamic acid, sulfhydryl or $-NH_2$;

10 R^2 is H, CF_3 ; or optionally substituted C_{5-6} aryl, C_{3-7} cycloalkyl, C_{5-7} heterocyclyl or together with R^3 an optionally substituted C_{3-4} alkylene group wherein L^3 and L^4 are single bonds thus forming a C_{5-6} ring fused with the aromatic ring to which L^3 and L^4 are attached;

15 R^3 is H; or optionally substituted C_{5-6} aryl, C_{3-7} cycloalkyl, C_{5-7} heterocyclyl or together with R^2 an optionally substituted C_{3-4} alkylene group wherein L^3 and L^4 are single bonds thus forming a C_{5-6} ring fused with the aromatic ring to which L^3 and L^4 are attached;

20 R^4 is H; or optionally substituted C_{5-6} aryl or C_{5-7} heterocyclyl;

R^6 is selected from H or optionally substituted C_{1-7} alkyl, C_{5-6} aryl and C_{1-4} alkylene- C_{5-6} aryl;

25 L^1 is optionally substituted C_{1-4} alkylene, C_{5-6} arylene, C_{1-4} alkylene- C_{5-6} arylene or $-L^5N(R^5)L^6-$, wherein L^5 and L^6

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are independently selected from optionally substituted C₁₋₄ alkylene and C₅₋₆ arylene, and R⁵ is H or C₁₋₄ alkyl;

L² is a single bond; or optionally substituted C₁₋₄ alkylene or -L⁷C(=O)L⁸-, wherein L⁷ and L⁸ are independently
5 selected from optionally substituted C₁₋₄ alkylene and a single bond; and

L³ and L⁴ are independently selected from a single bond, optionally substituted C₁₋₄ alkylene, -L⁹YN(OH)C(=O)L¹⁰- and -
L⁹C(=O)N(OH)YL¹⁰-, wherein L⁹ and L¹⁰ are independently

10 selected from optionally substituted C₁₋₄ alkylene, C₅₋₆ arylene, C₁₋₄ alkylene-C₅₋₆ arylene and a single bond, wherein Y is NH or a single bond; and

wherein the compound contains at least one -C(=O)N(OH)- group.

15 34. A compound according to claim 33 wherein at least one of R¹, L³ or L⁴ comprises a -C(=O)N(OH)- group.

20 35. A compound according to claim 33 wherein L⁴ comprises a -C(=O)N(OH)- group.

36. A compound according to any one of claims 33 to 35 wherein L⁴ is a L⁹-C(=O)N(OH)- group.

25 37. A compound according to claim 36 wherein L⁹ is selected from C₁₋₄ alkylene and C₅₋₆ arylene.

38. A compound according to claim 36 wherein L⁹ is methylene or phenylene.

30 39. A compound according to any one of claims 33 to 38 wherein X is CH.

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40. A compound according to any one of claims 33 to 39 wherein at least one of R^1 , R^2 and R^4 is H.

41. A compound according to any one of claims 33 to 39 wherein at least two of R^1 , R^2 and R^4 are H.

42. A compound according to any one of claims 33 to 39 wherein all of R^1 , R^2 and R^4 are H.

43. A compound according to any one of claims 33 to 42 wherein R^3 is optionally substituted C_{5-6} aryl.

44. A compound according to claim 43 wherein R^3 is phenyl.

45. A compound according to any one of claims 33 to 44 wherein R^6 is H or C_{1-7} alkyl.

46. A compound according to claim 45 wherein R^6 is H or C_{1-3} alkyl.

47. A compound according to any one of claims 33 to 46 wherein L^1 is phenylene, $-\text{CH}(\text{Ph})-$, $-\text{CH}_2\text{-phenylene-}$ or $-\text{CH}_2\text{C(=O)NH-phenylene-}$.

48. A compound according to any one of claims 33 to 47 wherein L^2 is a single bond or $-\text{C(=O)CH}_2-$.

49. A compound according to any one of claims 33 to 48 wherein L^3 is a single bond.